Table I. Yields of Baeyer-Villiger Product

ketone	ester	% yield[a]
4-heptanone	*n*-propyl butyrate	96
benzophenone	phenyl benzoate	83
p-bromoacetophenone	*p*-bromophenol	98
fluorenone	2'-hydroxydiphenyl 2-acid lactone	74
adamantanone	4-oxahomoadamantan-5-one	88
tetracyclone	tetraphenyl-α-pyrone	76

[a] Isolated yields except *n*-propyl butyrate which was quantitated by VPC.

into the above reaction vessel. After the mixture was cooled to −30 °C, with stirring, 25 mL of a 0.2 M solution of SO_3 in CH_2Cl_2 was added dropwise from the addition funnel over a period of 15 min, carefully maintaining the reaction mixture at −30 °C. The reaction progress was monitored by NMR, observing the appearance of the trimethylsilyl product signal as a singlet at δ 0.40. After completion of the reaction (ca. 30 min), this solution was utilized directly for the Baeyer–Villiger oxidations.

General Method for the Baeyer–Villiger Oxidation. To the above prepared solution of the bis(trimethylsilyl) monoperoxysulfate was added 1.4 mmol of the ketone to be oxidized in 10 mL of dry CH_2Cl_2 at −30 °C over 45 min. The reaction mixture was allowed to warm up to room temperature (ca. 30 °C) and kept at this temperature for 8 h. To the mixture was added 5 mL of H_2O, the solution was transferred to a separatory funnel, the aqueous layer was syphoned off, and the CH_2Cl_2 layer was washed with 2 × 20 mL of 5% aqueous $NaHCO_3$ and dried over $MgSO_4$. Rotoevaporation of the solvent and purification of the crude product by silica gel chromatography gave the results summarized in Table I. The identity of the products was confirmed by comparison of physical constants and IR and NMR spectra with the authentic materials.

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Registry No. Bis(trimethylsilyl) monoperoxysulfate, 23115-33-5; 4-heptanone, 123-19-3; benzophenone, 119-61-9; *p*-bromoacetophenone, 99-90-1; fluorenone, 486-25-9; adamantanone, 700-58-3; tetracyclone, 479-33-4; *n*-propyl butyrate, 105-66-8; phenyl benzoate, 93-99-2; *p*-bromophenol, 106-41-2; 2'-hydroxydiphenyl 2-acid lactone, 2005-10-9; 4-oxahomoadamantan-5-one, 21898-84-0; tetraphenyl-α-pyrone, 33524-67-3; bis(trimethylsilyl) peroxide, 5796-98-5; SO_3, 7446-11-9.

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A Mild Method of Hydrolysis of 2,4-Dialkoxy-6-substituted Pyrimidines to 6-Substituted Uracils

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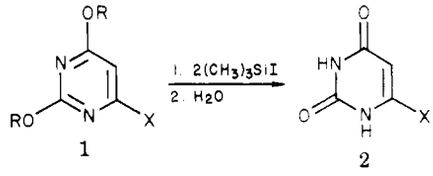
We are interested in synthesizing certain 6-substituted uracils for our enzymatic studies of new antitumor agents. Many of these compounds have been prepared by acid hydrolysis of the corresponding 2,4-dialkoxy-6-substituted pyrimidines;[1-3] however, the conditions required to hydrolyze these substituted pyrimidines can sometimes lead to decomposition of the products. For example, the hydrolysis of 2,4-dimethoxy-6-pyrimidinesulfonic acid with 0.1 N HCl was reported[1] to cause at least partial hydrolysis with loss of bisulfite to give barbituric acid. In our hands, under a wide variety of hydrolytic conditions, essentially all barbituric acid and little uracil-6-sulfonic acid was obtained. Acid hydrolysis of 2,4-dimethoxy-6-fluoropyrimidine was reported[2] to result in complete loss of fluoride ion, yielding only barbituric acid. The synthesis of 6-fluorouracil was later reported[4] in moderate yield by hydrogenolysis of 2,4-dibenzyloxy-6-fluoropyrimidine. Uracil analogues sometimes are protected as their corresponding 2,4-dialkoxypyrimidines in order to carry out chemical transformations on the ring. It is, then, important to have mild methods of deprotection to obtain the newly functionalized uracils. Since uracil-6-sulfonic acid was one of the compounds we wished to study, a mild hydrolysis method of 2,4-dimethoxy-6-pyrimidinesulfonic acid was sought. As a result of this investigation, we wish to report a general method of hydrolysis of 2,4-dialkoxy-6-substituted pyrimidines in high yields.

Table I. Hydrolysis of 2,4-Dialkoxypyrimidines by Iodotrimethylsilane[a]



1 2

compd no.	R	X	reaction time	% yield[b]
1a	CH_3	SO_3H	<15 min	quantitative
1b	CH_3	SO_2NH_2	<15 min	94
1c	CH_3	Cl	10 h	quantitative
1d	CH_3	CH_3	<15 min	87
1e	CH_3	F	6 h	67
1f[c]	C_2H_5	H	1 h	35
			2 h	53
			14 h	quantitative
1g	$C_6H_5CH_2$	Cl	<15 min	quantitative

[a] All reactions were carried out in dry sulfolane at 40–45 °C. [b] The yields are for crude products which had IR spectra identical with pure compounds. [c] There was no shift in the methylene resonances in the NMR spectrum during the reaction.

Iodotrimethylsilane has been used for the dealkylation of esters,[5] ethers,[6] and phosphate esters.[7] We have found that this reagent smoothly dealkylates 2,4-dialkoxypyrimidines to uracils in high yields. Table I summarizes the compounds used in the study, reaction times, and yields of products obtained.

It is interesting to note that unlike the reported aqueous acid hydrolysis of 2,4-dimethoxy-6-pyrimidinesulfonic acid,[1], iodotrimethylsilane dealkylation produces uracil-6-sulfonic acid in quantitative yield. The lower yield ob-

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tained with the 6-fluoro analogue probably is related to the inherent instability of 6-fluorouracil.[4] As was found in the dealkylation of esters by iodotrimethylsilane,[5] debenzylation in the pyrimidine series is much more facile than either demethylation or deethylation. The order of dealkylation appears to be benzyl > methyl > ethyl. 2,4-Diethoxy-6-chloropyrimidine (not listed in Table I) was dealkylated only to the extent of ca. 20% after 1 week under conditions that effected quantitative dealkylation of 2,4-dibenzyloxy-6-chloropyrimidine in less than 15 min. We have not investigated the mechanism of the hydrolysis, but it is most likely similar to that proposed by Jung and Lyster[5,6] for the hydrolysis of esters and ethers by iodotrimethylsilane. An alternate mechanism would involve initial attack of the pyrimidine nitrogens instead of the alkoxyl oxygens on iodotrimethylsilane.

Experimental Section

Melting points were determined on a Hoover-Thomas Unimelt melting point apparatus. Infrared spectra were obtained on a Perkin-Elmer 283 infrared spectrophotometer, and nuclear magnetic resonance (NMR) spectra were recorded on either a Hitachi Perkin-Elmer R20B or a Varian T-60 60 MHz spectrometer.

Sulfolane (Eastman) was dried by distillation from calcium hydride after pretreatment with sodium hydroxide pellets. The following compounds were synthesized according to the literature procedures and had physical and spectral properties consistent with their assigned structures: **1a**,[1] **1b**,[3] **1c**,[2] **1d**,[2,8] **1e**,[2] **1f**,[9] **1g**,[10] **2c**,[2,11] and **2e**.[4] 6-Methyluracil and uracil were purchased from Sigma Chemical Co.

General Procedure for the Hydrolysis of 2,4-Dialkoxy-6-substituted Pyrimidines. To a solution (or mixture) of the 2,4-dialkoxy-6-substituted pyrimidine (1.0 mmol) in dry sulfolane (2 mL) under nitrogen was syringed iodotrimethylsilane[6] (315 μL, 2.2 mmol). This was incubated at 40–45 °C[12] until the NMR resonance of the alkoxyl protons adjacent to the oxygens disappeared.[13] Water (10 mL) was added to the yellow to orange-red solution, and the cloudy solution was washed with 4 × 15 mL of methylene chloride or chloroform. The colorless aqueous layer was evaporated in vacuo to a white or off-white solid which was triturated with ether and collected by filtration. Spectral data were consistent with the assigned structures.

Uracil-6-sulfonic Acid (2a). The general procedure was followed, starting with 2,4-dimethoxy-6-pyrimidinesulfonic acid (1 mmol) which yielded uracil-6-sulfonic acid as an off-white solid (193 mg, quantitative). This was converted into the disodium salt[14] by adding 10 M NaOH to an ethanolic solution of this compound until no more solid precipitated. The precipitate was recrystallized from H_2O–EtOH to give white crystals. Physical and chemical properties of the product corresponded to those reported.[2] Anal. Calcd for $C_4H_2N_2O_5SNa_2 \cdot H_2O$: C, 18.91; H, 1.59; N, 11.02; S, 12.62. Found: C, 18.82; H, 1.64; N, 11.01; S, 12.61.

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Registry No. **1a**, 71885-70-6; **1b**, 21378-96-1; **1c**, 6320-15-6; **1d**, 7781-23-9; **1e**, 658-87-7; **1f**, 20461-60-3; **1g**, 71885-71-7; **2a**, 5807-21-6; **2b**, 5338-86-3; **2c**, 4270-27-3; **2d**, 626-48-2; **2e**, 591-36-6; **2f**, 66-22-8.

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(12) The reaction can be run at a higher temperature to increase the rate.
(13) At this concentration the sulfolane resonances do not interfere with the alkoxyl protons adjacent to the oxygen.
(14) It was found easier to purify this particular compound by first converting it to the disodium salt.

A Novel Synthesis of 2*H*-1,3-Benzoxathiol-2-ones

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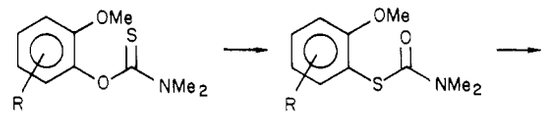
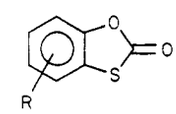
The synthesis of 2*H*-1,3-benzoxathiol-2-ones usually[1] is carried out either by thiocyanation of a substituted phenol,[2,3] by treatment of a 2-mercaptophenol with phosgene[2] or carbonyl sulfide,[4] or by hydrolysis of a 2-hydroxythiuronium salt,[5] the latter probably also involving an intermediate thiocyanate. These methods have the important disadvantage that the substitution pattern of the product is limited by the requirement of a substituent para to the phenolic hydroxyl to prevent para-directed thiocyanation. Further, in cases in which 2-mercaptophenols are used as starting materials, the use of phosgene or carbonyl sulfide presents a significant hazard in laboratories not equipped to deal with these materials. In view of these difficulties, an alternative method of preparation was desirable.

This report discusses the preparation of 2*H*-1,3-benzoxathiol-2-ones (**3**) by cyclization of the corresponding *S*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamates (**2**) which are conveniently available by means of the thione–carbamate rearrangement[6-8] of the corresponding *O*-(2-methoxyphenyl) *N*,*N*-dimethylthiocarbamates (**1**) as indicated in the equation. This rearrangement has been of



1a, R = H
b, R = 4-Me
c, R = 4-Cl
d, R = 3-OMe
e, R = 6-OMe

2a, R = H
b, R = 4-Me
c, R = 4-Cl
d, R = 3-OMe
e, R = 6-OMe



3a, R = H
b, R = 6-Me
c, R = 6-Cl
d, R = 7-OH
e, R = 4-OMe
f, R = 4-OH

considerable utility for the preparation of a variety of substituted mercaptobenzenes[9-15] and thus represents a

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